RECEIVED Application No. 10/659,063
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REMARKS

The Examiner continues to reject pending claims 1-6 and 8 as obvious over von Lund et al. This rejection is traversed for the reasons given below and reconsideration is respectfully requested.

In the Office Action, the Examiner stated that the Applicants' arguments in the previous paper were not found convincing as there is no limitation "that *requires* the said cADPR derivative *to be an agonist* (see claim 1)" (emphasis added). With respect, the Applicants point out that in the relevant language of claim 1:

> administering to said patient a therapeutically effective amount of a composition comprising cyclic adenosine diphosphate ribose (cADPR), or a functional analogue or derivative thereof,

the adjective "functional" modifies *both* nouns "analogue" and "derivative." Thus, Applicants again assert that the administered compound in the method of the invention is required to be cADPR or a compound *having the same function*, i.e., an *agonist* of cADPR. However, because of the Examiner's concern, claims 1 and 8 have been amended to recite "agonist" explicitly. Applicants submit that the meaning of these claims has in no way been changed by these amendments.

The Applicants' argument can be summarized as follows:

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- [0032], cited by the Examiner, includes a list of modulators, "such as agonists and antagonists," of CD38 enzyme activity and/or cADPR dependent responses that can be used in the Lund method and a list of treatable disorders. This second list includes *both* conditions where inflammation needs to be *treated* (as in the method of the instant invention) and conditions where inflammation needs to be *induced* (such as infections).

- As [0032] is not specific as to which modulator is suggested for which condition, it must be interpreted in conjunction with [0013].

- [0013], first half of the paragraph, states that CD38 *antagonists* may be used in the *treatment* of *inflammation* among other disorders.

- [0013], in the second half of the paragraph, states that *agonists* of CD38 should be used when the subjects are "infected with pathogenic microorganisms," i.e., a condition in which *inflammatory agents are recruited and inflammation is induced to fight the infection.*

- In Applicants' method, however, *agonists* are taught as useful for *fighting inflammation, not as useful for inducing it.*

- Thus, Lund et al. teaches the *exact opposite treatment* as in the Applicants' claimed method. Applicants submit that Lund et al. is a clear teaching away situation and that one of ordinary

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skill would never have been led to the Applicants' invention through any of the Lund et al. teachings.

- While not being bound by any theory, it is believed that these results are so different because the Applicants have based their claims on sound observation and direct testing of the effects of cADPR on inflammation itself, not on a removed effect. In contrast, Lund et al. created a totally artificial environment in their animal model by working with CD38KO mice, an environment that, from their results, clearly should not be extrapolated to clinical conditions.

The Applicants submit, therefore, that the rejection over Lund et al. has been overcome and that all claims are in condition for allowance. Such action is respectfully requested.

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The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the claims in the present application.

Respectfully submitted,

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